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09/701,453	04/16/2001	Dan M. Granoff	CHIR-0283	1041

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EXAMINER

DEVI, SARVAMANGALA J N

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 11/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/701,453

Applicant(s)

GRANOFF ET AL.

Examiner

S. Devi, Ph.D.

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 08/22/05.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 17-29 is/are pending in the application.
- 4a) Of the above claim(s) 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **RESPONSE TO APPLICANTS' AMENDMENT**

### **Applicants' Amendment**

- 1) Acknowledgment is made of Applicants' amendment filed 08/22/05 in response to the non-final Office Action mailed 02/22/05.

### **Status of Claims**

- 2) No claims have been amended via the amendment filed 08/22/05.  
Claims 17-29 are pending.  
Claims 17-28 are under examination.

### **Prior Citation of Title 35 Sections**

- 3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

### **Prior Citation of References**

- 4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

### **Rejection(s) Withdrawn**

- 5) The rejection of claim 17 and those dependent therefrom made in paragraph 8 of the Office Action mailed 02/22/05 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' arguments.

### **Rejection(s) Maintained**

- 6) The rejection of claims 17-23 and 25-27 made in paragraph 9 of the Office Action mailed 02/22/05 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992 - already of record) and van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996 - already of record) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record), is maintained for reasons set forth therein and herebelow.
- 7) The rejection of claims 24 and 28 made in paragraph 10 of the Office Action mailed 02/22/05 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-

698,1992 - already of record) as modified by van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996 - already of record) and Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record) as applied to claim 17 or 26 above, and further in view of Granoff (US 6,413,520, already of record) ('520), is maintained for reasons set forth therein and herebelow.

Applicants submit the following arguments. (a) To support an obviousness rejection under 35 U.S.C. § 103, all the claim limitations must be taught or suggested by the prior art. M.P.E.P. 2143.03. (b) The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on Applicant's disclosure. M.P.E.P. 706.02. (c) Costantino *et al.* fails to teach or suggest the use of immunogenic outer membrane vesicles from any strain of *Neisseria meningitidis*, nor the use of a combined vaccine comprising group C meningococcal oligosaccharides and antigens from group B *Neisseria meningitidis*. The reference of Costantino can be described as teaching away from the claimed invention in that Costantino suggests producing a protein-saccharide conjugate vaccine against serogroup B *N. meningitidis* by improving the immunogenicity of meningococcus B polysaccharide by coupling to an immunogenic protein (see page 691, col. 2). (d) The reference of van der Voort *et al.* fails to cure the deficiencies of Costantino *et al.* The reference of van der Voort *et al.* describes a hexavalent outer membrane vesicle vaccine against serogroup B *N. meningitidis*; however, fails to teach or suggest the use of a combined vaccine with serogroup C meningococcal oligosaccharides, nor provides any motivation for using a saccharide-based vaccine. (e) The reference of Paradiso *et al.* relied on as providing the motivation to combine the teachings of Costantino *et al.* and van der Voort *et al.* does not teach combining meningococcal C oligosaccharide conjugates with meningococcal B proteoliposomic vesicles, as recited in the claims, because Paradiso discusses only vaccines comprising meningococcal C polysaccharide conjugates and never discusses meningococcal C oligosaccharide conjugates. When Paradiso refers to mixing with the group C and/or group A conjugates, it is referring to the polysaccharide conjugates described in the article at pages 271-272 and Table 4, discussing only polysaccharides and polysaccharide conjugates. Paradiso cannot provide the motivation for combining an element that it never mentioned or referred to. (f) The showing that two references can be combined must be clear and particular. See *In re Dembiczak* (CA FC) 50 USPQ2d 1614 (4/28/1999). (g) The reference

of Granoff (US 6,413,520) also fails to cure the deficiencies of Costantino *et al.*, van der Voort *et al.*, and Paradiso *et al.* because Granoff also fails to teach or suggest any combination vaccine containing meningococcal C oligosaccharide conjugates and meningococcal B immunogenic outer membrane vesicles. (h) No prior art has been identified which specifically suggests combining MenB outer membrane vesicle antigens with MenC oligosaccharide conjugates as claimed. The Office has not met the burden of establishing a *prima facie* case of obviousness. (i) In the absence of some teaching or suggestion in the cited references concerning production of the claimed combination vaccine described in the present application, the Office has presented no more than an improper hindsight reconstruction of the present invention. As stated by the Court of Appeals for the Federal Circuit *In re Fine*, 5 USPQ2d 1596, 1600 Fed. Cir. 1988): one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

Applicants' arguments have been carefully considered, but are not persuasive. Applicants are reminded that Costantino *et al.*, Paradiso *et al.*, or van der Voort *et al.* are not anticipatory references applied under 35 U.S.C § 102, but are references applied under 35 U.S.C § 103. The reference of Costantino *et al.* does not teach away from the claimed invention, instead, teaches a conjugate vaccine comprising immunologically effective amounts of group C meningococcal oligosaccharides having a polymerization degree (DP) of up to 10 (i.e., about 12 repeating units) conjugated to CRM 197 and aluminium hydroxide adjuvant, and a method of inducing an immune response to group C *Neisseria meningitidis* by administering an immunologically effective amount of the vaccine to a subject (see page 693). van der Voort *et al.* is applied to document the disclosure of an immunogenic group B meningococcal hexavalent outer membrane vesicle vaccine from the group B meningococcal reference strain H44/76, which induced increased levels of bactericidal antibodies as well as a method of immunizing a mammal with the vaccine. van der Voort *et al.* also taught that the hexavalent vaccine advantageously covers more than 80% of the group B meningococcal subtypes isolated in many countries (see abstract; page 2745; Materials and Methods; Results; and Discussion). Granoff taught the routine use of polylactic acids and/or polyglycolic acids in combination with a meningococcal oligosaccharide conjugate. Granoff ('520) taught combining carriers, such as, polylactic and polyglycolic acids with meningococcal glycoconjugates for the purpose of primary vaccination wherein carriers do not themselves induce

the production of harmful antibodies (see lines 1-10 in column 6). Contrary to Applicants' contention, Paradiso *et al.* taught vaccines comprising meningococcal C oligosaccharide or saccharide conjugates. For example, one of the immunogenic meningococcal C conjugate vaccine described as having been tested in adults and children is the one described in reference 7 cited therein (see sentence bridging pages 271 and 272). Reference 7 is of Costantino *et al.* (*Vaccine* 10: 691-698, 1992), the same reference applied in the instant rejection, which taught group C meningococcal oligosaccharide conjugate. The very next sentence on page 272 of Paradiso's reference states as follows: 'We have similarly prepared glycoconjugates prepared using these 'saccharides' covalently linked to the carrier CRM197'. References 8 and 9 cited therein describe meningococcal C polysaccharide conjugates. Therefore, when Paradiso refers to mixing with 'the group C and/or group A conjugates', Paradiso is referring to the group C meningococcal oligosaccharide conjugate or the group C meningococcal polysaccharide conjugate. Therefore, Applicants' argument that Paradiso cannot provide the motivation for combining an element that it never mentioned or referred to, is incorrect. The term 'saccharides' referred to by Paradiso encompasses oligosaccharides (see page 170 of *Glossary of Biochemistry and Molecular Biology*. (Ed) Glick, D.M. Portland Press, London, 1997). Paradiso does indeed provide the express motivation for combining the group C meningococcal oligosaccharide conjugate mentioned therein with the group B meningococcal outer membrane vesicles. Therefore, Paradiso specifically suggests combining MenB outer membrane vesicle antigens with a MenC oligosaccharide conjugate as claimed. Contrary to Applicants' assertion, the teaching or suggestion to make the claimed combination and the reasonable expectation of success both are found in the prior art and are not based on Applicant's disclosure. The Office has clearly met the burden of establishing a *prima facie* case of obviousness. With regard to Applicants' allegation of improper hindsight reconstruction, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). '[F]or the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific

references'. *In re Nilssen*, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988). The rejection stands.

### Remarks

8) Claims 17-28 stand rejected.

9) **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses or papers is (571) 273-8300.

11) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.Mov>. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

Serial No. 09/701,453  
Art Unit: 1645

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

November, 2005

  
S. DEVI, PH.D.  
PRIMARY EXAMINER